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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,240	03/23/2004	Giovanni Caponetti	250893US0CONT	1764

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/806,240	CAPONETTI ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☒ Claim(s) *1-21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 10/030,686.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/22/04;3/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are pending.

Information Disclosure Statement

Receipt of the IDS's submitted on September 22,2004 and March 23, 2004 is acknowledged. The last page of the IDS filed on 9/22/04 was not a proper PTO-1449 form and was not considered.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The claims are objected to because the lines are crowded too closely together, making reading difficult. Substitute claims with lines one and one-half or double spaced on good quality paper are required. See 37 CFR 1.52(b).

Claims 14-20 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only, and/or, and cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 14-20 have not been further treated on the merits.

The use of the trademarks PULVINAL® (pg. 22, line 25; pg. 23, line 10; and pg. 26, line 19) and TURBULA® (pg. 22, lines 11 and 18; Example 5 on pg. 29) have been noted in this

application. Trademarks should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 4, 10-13, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is vague and indefinite, because said claim recites a "starting diameter," which implies that the diameter listed in said claims will change. Therefore, a person of ordinary skill in the art would not be able to ascertain what particle diameters define the metes and bounds of the particles claimed in claim 4. It is noted that claim 4 is a composition claim and not a product-by-process claim, as such; a skilled artisan would have no expectation that fundamental composition characteristics, such as particle diameter would change.

Claim 10 is vague and indefinite because it is unclear whether the items contained within parentheses were intended as additional claim limitations, or merely as examples.

Claim 12 is vague and indefinite, because a person of ordinary skill in the art at the time of the instant invention would not be able to determine the meaning of the phrase "substantially

free from fine particles." It is noted that the word "substantially" is not defined in the specification.

Claim 21 is vague, because it is unclear what is meant by the term "active principles." This term is not defined in the specification. Therefore, a skilled would be unable to ascertain what is the difference, if any, between an active ingredient and an "active principle" and as a result the intended metes and bounds of said claim would remain ambiguous.

The remaining claims are rejected for depending upon a rejected claim.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4, and 14-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Ganderton et al. (U.S. Patent No. 5,254,330).

Applicant claims particles for use as a carrier with a median diameter greater than 90 microns and a surface rugosity ≤ 1.1, wherein the particles consist of one or more saccharides selected from glucose, mannose, galactose, sorbitol, mannitol, lactose, saccharose, trehalose, raffinose, and cyclodextrins.

Ganderton discloses in claim 1 a dry powder inhaler composition comprising (a) an effective amount of a non-proteinaceous active agent in admixture with a **carrier**; wherein said carrier comprises **particles having an average particle size ranging from 5.0-1,000 microns and a rugosity of less than 1.75**. The average particle size and rugosity ranges claimed by Ganderton overlap with the median diameter and rugosity range claimed by the Applicant. In claims 6 and 8, Ganderton discloses that the powders may contain active agents, including **beta-**

agonists, steroids, and sodium chormoglycate. In claims 2 and 12, Ganderton discloses that the carrier is a crystalline sugar selected from **glucose**, fructose, **mannitol**, sucrose, and **lactose**. In Example 1, Ganderton discloses that the **rugosity** of crystalline lactose decreased after recrystallization from a value of 2.36 to a **value of 1.16**. Ganderton discloses that the **average particle size of the pharmacological agents** incorporated in his invented compositions more preferably range from **0.5 microns to 5.0 microns** and at least 95% of the particles should have a size within these preferred ranges (col. 3, lines 32-38). Specific examples of suitable, beta-agonists, anticholinergics, and steroids for use in Ganderton's compositions include, **ipratropium bromide (anticholinergic), oxitropium bromide (anticholinergic), salbutamol (beta-agonist), terbutaline (beta-agonist), beclomethasone dipropionate (anti-inflammatory steroid), and budesonide (anti-inflammatory steroid)** (col. 3, lines 58-65). It is the Examiner's position that Ganderton inherently discloses a method of producing pharmaceutical preparations comprising the step of combining a carrier and one or more active ingredients having a median diameter $\leq$ 6.4 microns, wherein the active ingredient is a beta-agonist, an anti-inflammatory steroid, or an anticholinergic, because his compositions comprise both a carrier and an pharmaceutically active agent. The carrier and active agent of Ganderton's invented compositions could only both be present in the same composition if they had been combined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5, 8-10, and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ganderton et al. (U.S. Patent No. 5,254,330) in view of Kato et al. (EP 0786526; IDS).

Applicant Claims

Applicant claims (a) particles for use as a carrier with a median diameter greater than 90 microns and a surface rugosity ≤ 1.1, (b) a method for the preparation of smooth carrier particles (claims 9-13), and (c) a method for the preparation of pharmaceutical formulations (claims 14-20).

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Ganderton have been set forth above. Kato teaches lactose spherical particles and processes for their production comprising a step of **charging crystalline lactose and/or lactose granules onto a rotary disk** in the **treatment vessel** (i.e. container) of a centrifugal tumbling apparatus, dispersing powdered lactose to the lactose granules and/or crystalline lactose as the rotary disk is rotated while providing slit air into the vessel, **while also spraying water, an aqueous lactose solution or a dilute aqueous solution of a water-soluble polymer**, and a fixation treatment step of drying the obtained spherical particles in a fluidized bed apparatus while spraying an aqueous lactose solution and/or a dilute solution of a water-soluble polymer (title and abstract). The crystalline lactose serving as the nuclei according to the invention is crystalline lactose, preferably with a **particle size between 150 microns and 300 microns** (col. 3, lines 50-53). The lactose particles preferably have a preferred abrasiveness no greater than 1.0%, most preferably no greater than 0.5% (col. 5, lines 1-3). Abrasiveness reads on roughness and rugosity. The production of the lactose particles of Kato's invention may be practiced using a CF granulator, depicted in Figure 1, and comprising a granulation vessel (i.e. container), spray nozzle, rotary disk, etc (Figure 1 and col. 11, lines 5-24). A rotary disk reads on a rotating paddle. The aqueous water-soluble polymer solutions have a polymer concentration of 2.5% (Example 3), and suitable water-soluble polymers include, cellulose polymers such as **carboxymethyl cellulose**, **methylcellulose**, **hydroxyethyl cellulose**, and synthetic polymers such as **polyvinylpyrrolidone**, etc. (col. 5, lines 12-17). Kato teaches that the suitable concentration of the dilute water-soluble polymer is determined experimentally for each water-soluble polymer (col. 5, lines 19-24).

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Ganderton lacks the teaching of a method of producing smooth carrier particles utilizing a granulator and compositions comprising water-soluble polymer additives. These deficiencies are cured by the teachings of Kato.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Ganderton and Kato, because Ganderton teaches dry powder medicinal compositions comprising particles of a saccharide carrier (e.g. lactose) and Kato teaches a method of producing smooth lactose carrier particles utilizing a granulator. A skilled artisan would have been motivated to combine the teachings of Ganderton and Kato, because Kato's disclosed method and granulator would have provided the artisan with a suitable method and device for the preparation of Ganderton's compositions, also comprising a carrier. For these reasons, a skilled artisan would have had a reasonable expectation of success upon combing the teachings of the prior art.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ganderton et al. (U.S. Patent No. 5,254,330) in view of de Haan et al. (U.S. Patent No. 5,382,434) (USPN '434).

Applicant Claims

Applicant claims particles for use as a carrier with a median diameter greater than 90 microns and a surface rugosity ≤ 1.1, wherein the carrier particles consist of alpha-lactose monohydrate.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Ganderton have been set forth above. USPN '434 teaches dry pharmaceutical preparation containing potent steroidal medicinal agents in combination with an excipient capable of binding the agent (i.e. a carrier), including spray dried polyalcohols, granulated **alpha-lactose monohydrate**, and mixtures thereof (abstract). In Example VI de Haan teaches that commercially available alpha-lactose monohydrate (PHARMATOSE® M100) had a binding percentage of 64.7% for ethinyl estradiol (EE), a steroid, and lost less of the bound EE upon sieving (col. 10, lines 10-14).

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Ganderton lacks the teaching of alpha-lactose monohydrate. This deficiency is cured by the teachings of de Haan.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Ganderton and de Haan, because both inventors

teach carriers comprising lactose. A skilled artisan would have been motivated to combine the teachings of Ganderton and de Haan, because alpha-lactose monohydrate was shown by de Haan to have a superior binding percentage of a steroidal active agent and exhibited less loss of active agent upon sieving than other carriers. A skilled artisan would also have been motivated to combine the prior art teachings, because alpha-lactose monohydrate is a commercially available pharmaceutically acceptable lactose carrier. For these reasons, a person of ordinary skill in the art would have had a reasonable expectation of success upon combination of the prior art teachings and modification of Ganderton's compositions to utilize, specifically alpha-lactose monohydrate.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 9-20 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 5, and 8-16 of U.S. Patent No. 6,641,844

(USPN '844). It is noted that USP '844 has the same assignee as the instant application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of USPN '844 are obvious over the claims of the instant application, because the claim limitations are substantially similar. The claims of USPN '844 recites a process for modifying the surface properties of particles for use as a carrier having a starting diameter of 90-150 microns, consisting of alpha-lactose monohydrate (claim 8), additives (claim 9) selected from lubricants (claims 9 and 11), anti-adherents, and glidants wherein after said process one or more active agents are added to the carrier, including beta-agonists (claim 13), anti-inflammatory steroids (claim 14), and anticholinergics (claim 15). The process of USPN '844 utilizes a mixer, which reads on a granulator, wherein the mixing time ranges from 5-360 minutes (claim 5). Therefore, the Examiner concludes that the cited claims of the instant application are *prima facie* obvious over the cited claims of USPN '844.

All claims are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over all claims of U.S. Patent No. 6,780,508 (USPN '508). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of USPN '508 are obvious over the claims of the instant application, because they collectively have the same limitations. Both claim sets recite carriers coated with an additive, having a median diameter greater than 90 microns and a rugosity that is less than or equal to 1.1. Additionally, both claim sets recite the same Markush groups of water-soluble polymers, additives, lubricants, and anti-adherents.

Claims 1-6 and 21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7-10, and 13-15 of U.S. Patent No. 6,884,794 (USPN '794). It is noted that USP '794 has the same assignee as the instant application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of USPN '794 are obvious over the claims of the instant application, because the claim limitations are substantially similar. USPN '794 recites a medicinal powder comprising (i) a fraction of fine particles comprising particles of a pharmaceutically acceptable excipient and magnesium stearate, having a mean particle size of less than 35 microns, (ii) a fraction of course particles comprising particles of a carrier having a particle size of at least 100 microns, and (iii) one or more micronized active ingredients selected from the group consisting of formoterol (beta agonist), budesonide (corticosteroid), TA 2005 (beta agonist), stereoisomers, salts, and/or epimers, and mixtures thereof. USPN '794 also recites that the carrier particles have a fissure index of at least 1.25, which is comparable to a rugosity of 1.1 or less. Both claim sets also claim compositions comprising excipients, including crystalline sugars (e.g. alpha-lactose monohydrate). Therefore, the Examiner concludes that the cited claims of the instant application are *prima facie* obvious over the cited claims of USPN '794.

Other Matter

The Examiner respectfully suggests insertion of the U.S. Patent number of the instant application's parent in the first line of the specification.

Conclusion

Claims 1-21 are objected and rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0664. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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